REMARKS

Claims 1-40, of which claims 1-2, 9-11, 18, 21-22, and 29 are currently amended, are pending and appear in this application for the Examiner's review and consideration. Claims 1-2, 10-11, and 21-22 are amended for definiteness, and claims 9, 18, and 29 are amended to correct an informality. The specification is amended to include correct references to FIGS. 11A-B and 14A-D, and to correct a typographical error in TABLE 2. As no new matter is added, entry of the amendments at this time is respectfully requested.

Claims 21-40 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement for the reasons set forth on pages 2-3 of the Office Action. Applicants respectfully traverse.

First, Applicants would like to note that the knowledge available in the relevant field of art, *i.e.*, the field of medicinal cannabinoids, discloses the therapeutic activities attributed to the compounds of the present invention. In particular, the THC-type cannabinoid dexanabinol, which can be considered the parent compound of the present derivatives, was shown to possess such therapeutic activities, as demonstrated in, for example, U.S. Patent Nos. 4,876,276; 5,284,867; 5,521,215; 5,932,610; 6,331,560; and 6,545,041. These references, other than U.S. Patent Nos. 6,331,560 and 6,545,041, which are continuations of U.S. Patent No. 5,932,610, are cited in the present specification (*see* published application, at paragraphs [0009], [0012]).

Building on this background knowledge, the Physiological Examples in the specification provide additional support for the efficacy of the present compounds. Physiological Example 1 demonstrates that compounds of the invention can specifically bind to the NMDA receptor. As known in the art, the NMDA receptor has been widely investigated as a target for pharmacological management of pain and a variety of neurological disorders and central nervous system (CNS) degeneration. In particular, excessive or insufficient activation of NMDA receptors have been implicated in aberrations of normal CNS development in the development of epilepsy, in the neurodegeneration associated with Parkinson's, Alzheimer's, and Huntington's diseases, and with amyotrophic lateral sclerosis (ALS). NMDA antagonists were reported to alleviate excitotoxic neuronal death observed after head injury, ischemic events, hypoxia, and hypoglycemia, and to reduce

tolerance of or dependence on drugs of abuse. (*See* Rogawski, *Trends in Parmacol. Sci.* 14:325-331 (1993); Danbolt, *Progress in Neurobiology* 65:1-105 (2001)). Thus, the results provided in Physiological Example 1 support use and efficacy of the present compounds in treating and preventing damages caused by ischemia, injuries to the central nervous system, neurodegenerative disorders, pains, and drug abuse, tolerance or dependence.

The specification further supports and explains such neuroprotective activities in Physiological Example 4 (showing the effect of PRS-211 compounds on cerebral edema in a rat model of closed head injury, as mimicking of human brain injury); Physiological Examples 5 and 6 (showing neuroprotection by PRS-211 compounds in transient Middle Cerebral Artery Occlusion, as mimicking of human stroke and ischemia); Physiological Example 7 (showing neuroprotection by dexanabinol analogs in the MPTP model of Parkinson's Disease); and Physiological Example 10 (showing prevention and reversal of tolerance to morphine). In addition, Physiological Example 2 (directed to an ear edema model of inflammation) and Physiological Example 3 (directed to inhibition of inflammatory mediators in LPS stimulated macrophages) demonstrate anti-inflammatory and immunomodulatory activities of the present compounds, while Physiological Example 9 (a rat model of myocardial ischemia) supports efficacy of the present compounds in treating cardiovascular disorders.

Preventive functions of the present compounds are also shown in the examples, Physiological Examples 2, 4 and 9 in particular, in which the compounds are administered before the injury as prophylactic agents.

Further, the correlation of the present Physiological Examples to treatment and/or prevention of the diseases or disorders in humans, as specifically noted above for Physiological Examples 4-6, is known in the art. Since a person skilled in the art would recognize the particular models provided in the specification as correlating to the conditions recited in claims 21-40, the present specification provides sufficient working examples and satisfies the enablement requirement of § 112, first paragraph (*see* MPEP 2164.02).

Applicants therefore respectfully submit that the Physiological Examples provided in the specification demonstrate efficacy of the present compounds in treating and preventing a wide range of diseases and disorders, including those recited in claims 21. The language in the specification at page 6, line 6 to page 7, line 15 is not "prophetic at best" or does not

"merely describe[] applicants' intent for the compound," as the Examiner states, but is enabled, for example by the Physiological Examples, which show efficacy of the present compounds in various studies and models corresponding to, or mimicking, human diseases and disorders.

Accordingly, Applicants respectfully submit that the present specification provides sufficient support for use of the compounds in treatment and/or prevention as recited in the claims, such as to enable a skilled artisan to make and/or use the invention. Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

Claims 1, 2, 10-11, and 21-22 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the reasons stated on pages 4-5 of the Office Action. In response, Applicants have made appropriate corrections in these claims. Claims 1, 10, and 21 are amended to clarify that: (a) the recited carbon side chain comprises 1-8 carbon atoms and 1-3 heteroatoms, with at least one heteroatom being placed between two carbon atoms; and (b) the recited cyclic moiety or aromatic or heterocyclic moiety has from 5-20 atoms comprising one or two-ringed structure, wherein each ring comprises 3-8 carbons and 0-4 heteroatoms. The heteroatoms are also identified in the claims. The ring structure can comprise zero heteroatom because it may be an aromatic moiety. The recitation "interrupted by" is deleted for clarity because any heteroatom in a heterocycle will necessarily be placed between carbon atoms. Claims 2, 11, and 22 are similarly amended. Claim 9, 18, and 29 are amended and now presented in a proper Markush format.

Therefore, all rejections under 35 U.S.C. § 112, second paragraph, should be withdrawn.

Claims 3-8, 12-17, and 19-20 are objected to as being dependent upon a rejected base claim, but are noted as allowable if rewritten in independent form. Since the base claims are appropriately amended as explained and are now believed to be allowable, there is no need to re-write these claims in independent form. Accordingly, the objection to these dependent claims has been rendered moot and should also be withdrawn.

In view of the above, the entire application is believed to be in condition for allowance, early notification of which would be appreciated. Should the Examiner not agree, a personal or telephonic interview is respectfully requested to discuss any remaining issues in order to expedite the eventual allowance of the claims.

Respectfully submitted,

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